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EXAMINER	
KERR, KATHLEEN M	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 02/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/941,945	BATHE ET AL.	
	Examiner	Art Unit	
	Kathleen M Kerr	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *12,14,16,19,23-25 and 29-35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12,14,16,19,23-25 and 29-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/17/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Application Status

1. In response to the previous Office action, a non-Final rejection (mailed on September 23, 2003), Applicants filed a response and amendment received on November 17, 2003. Claims 1-11, 13, 15, 17, 18, 20-22, and 26-28 were cancelled, Claims 12, 14, 16, 19, 23, 24, and 25 were amended, and Claims 29-35 were added. Thus, Claims 12, 14, 16, 19, 23-25, and 29-35 are pending in the instant Office action and will be examined herein.

Priority

2. As previously noted, the instant application is granted the benefit of priority for the foreign application 10043331.6 filed in Germany on September 2, 2000 as requested in the declaration. Receipt is acknowledged of papers submitted under 35 U.S.C. § 119(a)-(d), which papers have been placed of record in the file. Said papers are not in English.

Additionally, the Examiner noted that DE 10043331 discloses a sigD gene that is not identical to the sigD gene of the instant application; thus, the effective filing date of the pending claims is August 30, 2001 (the application's filing date).

Information Disclosure Statement

3. The information disclosure statement filed on November 17, 2003 has been reviewed, and its references have been considered as noted on the attached copy.

Withdrawn - Objections to the Specification

4. Previous objection to the specification because the title is not descriptive is withdrawn by virtue of Applicants' amendment.

5. Previous objection to the Abstract for not completely describing the disclosed subject matter is withdrawn by virtue of Applicants' amendment.

6. Previous objection to the specification for containing out-dated U.S. serial number 09/396,478 on page 14, paragraph [0042] is withdrawn by virtue of Applicants' amendment.

Maintained - Objections to the Specification

7. Previous objection to the specification for being confusing concerning the phrase on page 6, paragraph [0024], "enzyme sigma factor D". Applicants argue that it is clear and comment that supporting information has been filed. No such information has been received. Applicants comment that this clearly refers to an RNA polymerase involved in transcription; however, no mention of RNA polymerases is noted in the specification. Clarification is required.

Withdrawn - Objections to the Claims

8. Previous objection to Claims 20 and 21 under 37 C.F.R. § 1.75 as being duplicate claims of one another and of Claim 13 is withdrawn by virtue of Applicants' cancellation of Claims 20 and 21.

9. Previous objection to Claim 25 under 37 C.F.R. § 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim is withdrawn by virtue of Applicant's amendment.

Withdrawn - Claim Rejections - 35 U.S.C. § 112

10. Previous rejection of Claims 12-25 under 35 U.S.C. § 112, second paragraph, as being indefinite for the phrase "the sigD gene or nucleotide sequences coding for the sigD gene" is withdrawn by virtue of Applicants' amendment requiring a specific structure of the sigD gene in each occurrence.

11. Previous rejection of Claims 15-16 under 35 U.S.C. § 112, second paragraph, as being indefinite for the added step in Claim 15 is withdrawn by virtue of Applicants' cancellation of Claim 15 and amendment to Claim 16 to depend directly from Claim 12 with a clearly added limitation of an additional method step.

12. Previous rejection of Claims 17-18 under 35 U.S.C. § 112, second paragraph, as being indefinite for the metes and bounds of the cited "pathways" is withdrawn by virtue of Applicants' cancellation of said claims.

13. Previous rejection of Claims 20-21 under 35 U.S.C. § 112, second paragraph, as being indefinite for the phrase "expression … is enhanced" is withdrawn by virtue of Applicants' cancellation of said claims.

14. Previous rejection of Claim 22 under 35 U.S.C. § 112, second paragraph, as being indefinite for the term "regulatory properties" of the sigD polypeptide is withdrawn by virtue of Applicants' cancellation of said claim.

15. Previous rejection of Claims 23-24 under 35 U.S.C. § 112, second paragraph, as being indefinite for the listed genes being shown as "**the** gene dapA" for example (emphasis added) is withdrawn by virtue of Applicants' amendment.

16. Previous rejection of Claim 23 under 35 U.S.C. § 112, second paragraph, as being indefinite for the phrase "the gene lysE coding for lysine export" is withdrawn by virtue of Applicants' amendment.

17. Previous rejection of Claims 12-25 under 35 U.S.C. § 112, first paragraph, written description, is withdrawn by virtue of Applicants' amendment limiting the sigD gene to a specific structure or genus of structures (anything encoding SEQ ID NO:2 is a closed genus of structures).

18. Previous rejection of Claims 13, 17, 18, 23, and 24 under 35 U.S.C. § 112, first paragraph, scope of enablement, is withdrawn by virtue of Applicants' cancellation and/or amendment of said claims.

19. Previous rejection of Claim 22 under 35 U.S.C. § 112, first paragraph, enablement, is withdrawn by virtue of Applicants' cancellation of said claim.

Maintained - Claim Rejections - 35 U.S.C. § 112

20. Previous rejection of Claim 23 under 35 U.S.C. § 112, first paragraph, scope of enablement, is maintained. Applicants' arguments have been fully considered but are not deemed persuasive for the following reasons.

Applicants argue that they need not describe every possible embodiment of the invention; the Examiner does not disagree. However, what the specification must do, in combination with the art, is to describe so as to enable the production of the genus of feedback-resistance aspartate kinases and threonine dehydratases. A single example of both enzymes is described in the specification. No description of what makes these enzymes feedback-resistant is described. Thus, being able to predictably produce other members of this genus is not enabled by the specification.

Withdrawn - Claim Rejections - 35 U.S.C. § 102

21. Previous rejection of Claims 12-16, 19-21, and 25 under 35 U.S.C. § 102(b) as being anticipated by Kimura *et al.* is withdrawn by virtue of Applicants' amendment.

NEW ISSUES

Claim Objections

22. Claim 29 is objected to under 37 C.F.R. § 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 12 requires the use of the full-length of SEQ ID NO:1 while Claim 29 attempts to only require use of the open reading frame of 301-864 of SEQ ID NO:1. Since less required sequence is equivalent to broader scope, Claim 29, fails to further limit the claimed subject matter effectively.

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

23. Claims 23 and 24 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In these claims, various additional genes are noted. The inclusion of both the gene name (or abbreviation) and the enzyme name is confusing. For example, if a gene for glucose-6-phosphate dehydrogenase was named gpd and not "zwf" as required in the claims, would this read on the claim or not? Many genes are incorrectly identified during genome projects and the like, thus using gene names to identify any gene encoding a particular enzyme is confusing. The Examiner suggests removal of the gene name limitation entirely.

Also in Claims 23 and 24, the nature of the following proteins is unclear: "a protein for lysine export", "a Zwa1 protein", and "a Zwa2 protein". These proteins are unclear as to their metes and bounds from simply their name or their function. While the specification gives references for specific examples of these proteins, no limitation to these specific proteins can be read into the specification. Thus, one of skill in the art would unclear as to the genus of genes encoding a protein for lysine export, for example. Clarification is required.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

24. Claim 23 is rejected under 35 U.S.C. § 112, first paragraph, written description, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 23 is drawn to a method optionally using genes for feedback-resistant aspartate kinase and feedback-resistant threonine dehydratase wherein said gene is claimed solely by function and without any structural limitations.

The Court of Appeals for the Federal Circuit has recently held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as be structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." University of California v. Eli Lilly and Co., 1997 U.S. App. LEXIS 18221, at *23, quoting Fiers v. Revel, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original). To fully describe a genus of genetic material, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these.

In the instant specification, a single example of both feedback-resistant enzymes is described in the specification. No description of what makes these enzymes feedback-resistant is described. Thus, one of skill in the art would be unable to predict the structure of other genes encoding these feedback resistant enzymes. Therefore, claims drawn to methods using said genes are not adequately described.

25. Claims 23-24 are rejected under 35 U.S.C. § 112, first paragraph, written description, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 23-24 are drawn to a method optionally using genes for proteins by name only wherein said gene is claimed solely by function and without any structural limitations.

The Court of Appeals for the Federal Circuit has recently held as described above. While genes encoding known enzymes with particular functions, such as genes encoding dihydrodipicolinate synthase, are adequately described by virtue of their specification function and their examples in the art, this is not the case for genes encoding proteins without clear support in the art for their genus: a protein for lysine export, Zwa1 protein, and Zwa2 protein. The mere name of these proteins does NOT connote a structure and/or function as is the case with the specific enzymes noted elsewhere in the claims. One example of each is noted in the specification; however, no description of how to maintain Zwa1-like protein structure and/or function is found. Thus, one of skill in the art would be unable to predict the structure of other members of the genus of genes claimed.

26. Claims 12, 14, 16, 19, 23-25, 29-35 are rejected under 35 U.S.C. § 112, first paragraph, scope of enablement, because the specification, while being enabling for overexpressing SEQ ID NO:1 by transforming a host cell with a vector comprising SEQ ID NO:1 and a promoter, does not reasonably provide enablement for overexpressing SEQ ID NO:1 by means otherwise mentioned in the specification. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. To practice the claimed invention to the full extent of its scope would require undue experimentation.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The Court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the

breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

In the specification on pages 10-11 (paragraph [0036]), means of overexpression are described. Said means include not only increasing the copy number of a gene or regulating the gene with a particular promoter, which means are enabled by the art, but also include altering the ribosome binding site, altering the lifetime of the mRNA, altering the protein so as to prevent degradation, and altering media conditions, all of which are known in the art to "overexpress" a gene in specific examples, but none of which are predictable with sigD or other genes that lack specific examples in the art. The specification provides no working examples or direction for overexpression using means of ribosome binding site, altering the lifetime of the mRNA, altering the protein so as to prevent degradation, and altering media conditions. The nature of the invention is that these means are specific to a particular gene sequence and cannot be extrapolated from other, unrelated genes; there is no particular recipe of media that will overexpress all genes. Thus, overexpression using these methods is wholly unpredictable and not enabled by the specification or the art.

Claims 19 and 33 are included in the instant rejection because the use of the vector does not limit the concept of "overexpression" in Claims 12 and 31, respectively. Claim 30 is included in the instant rejection because the vector is not limited to SEQ ID NO:1 with a promoter which controls the overexpression, thus leaving the option for overexpression by other means as noted above.

27. Claims 23-24 are rejected under 35 U.S.C. § 112, first paragraph, scope of enablement, because the specification, while being enabling for methods using known zwa1, zwa2, and lysC

genes as described in the specification, does not reasonably provide enablement for methods using other of these genes. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. To practice the claimed invention to the full extent of its scope would require undue experimentation.

The factors to be considered in determining whether undue experimentation is required are summarized.

The instant specification teaches particular examples of lysC, zwa1, and zwa2 from the art. The art fully enables using these particular genes. While the instant specification describes and enables means for identifying other lysC, zwa1, and zwa2 genes using hybridization methods, etc., these methods do not enable one of skill in the art to make all, or a relevant portion of, the polynucleotides within the scope of the claims because the ability to find a lysC, zwa1, and zwa2 gene, which is structurally related said sequences, is not equivalent to the ability to make a lysC, zwa1, and zwa2 genes as required by the statute (i.e., "make and use"). No description in the specification or the art provides particular residues whose encoding is important within the disclosed sequence so that its lysC-, zwa1-, and zwa2-nature is maintained. Thus, one of skill in the art would be unable to predict the structure of the other members of the genus in order to make such members. Therefore, the instant claims are not enabled to the full extent of their scope.

Examiner's Comments

28. As previously noted, Applicants have not overexpressed the sigD gene, SEQ ID NO:1, encoding a 188 amino acid protein (SEQ ID NO:2), in coryneform to produce L-lysine in

culture. However, the Examiner has no evidence to indicate that overexpression of sigD will abolish the lysine production already in coryneform. No requirement that overexpression of sigD *increases* amino acid production in coryneform need be meet for the pending claims. Thus, the claims are enabled for such methods, which methods have utility since amino acids are important nutritional additives.

Also as previously noted, Nakagawa *et al*. (EP 1108790, see IDS) disclose the entire genome of *C. glutamicum*. Nakagawa *et al*. teach SEQ ID NO:1 but do not define the sequence as encoding the protein that is SEQ ID NO:2, let alone describe the region as encoding a sigD protein. The coding sequence of SEQ ID NO:1 spans two defined open-reading frames taught by Nakagawa *et al*. (see page 52 and attached alignment) encoding an epoxide hydroxylase and a hypothetical membrane protein.

Also as previously noted, the coding sequence of SEQ ID NO:1 of the instant application does not start with the usual "atg" codon for a methionine, but starts with a "ttg" codon, which typically encodes internal methionine residues in proteins. However, in view of the disclosed definition of sigD as an RNA polymerase factor, the Examiner was able to establish similarities between SEQ ID NO:2 and other coryneform sigD proteins of similar size recently disclosed in the art.

Summary of Issues Pending

29. The following is a summary of the issues pending in the instant application:

a) The specification stands objected to for being confusing concerning the phrase on page 6, paragraph [0024], "enzyme sigma factor D". .
b) Claim 29 stands objected to under 37 C.F.R. § 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim.

c) Claims 23 and 24 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for the inclusion of both the gene name (or abbreviation) and the enzyme name being confusing and for "a protein for lysine export", "a Zwa1 protein", and "a Zwa2 protein".
d) Claim 23 stands rejected under 35 U.S.C. § 112, first paragraph, written description (feedback-resistant enzymes).
e) Claims 23-24 stand rejected under 35 U.S.C. § 112, first paragraph, written description, for "a protein for lysine export", "a Zwa1 protein", and "a Zwa2 protein".
f) Claims 12, 14, 16, 19, 23-25, 29-35 stand rejected under 35 U.S.C. § 112, first paragraph, scope of enablement, for overexpressing.
g) Claim 23 stands rejected under 35 U.S.C. § 112, first paragraph, scope of enablement (feedback-resistant enzymes).
h) Claims 23-24 stand rejected under 35 U.S.C. § 112, first paragraph, scope of enablement, for zwa1, zwa2, and lysC genes.

Conclusion

30. Claims 12, 14, 16, 19, 23-25, 29-35 are not allowed for the reasons identified in the numbered sections of this Office action. Applicants must respond to the objections/rejections in each of the numbered sections in this Office action to be fully responsive in prosecution.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kathleen M Kerr whose telephone number is (571) 272-0931. The examiner can normally be reached on Monday through Friday, from 9:00am to 6pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathupura Achutamurthy can be reached on (571) 272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Kathleen M Kerr
Examiner
Art Unit 1652

February 18, 2004